LISTING OF CLAIMS

1. (Original) A compound of formula (I),

$$\begin{array}{c}
R^4 \\
R^5
\end{array}$$

$$\begin{array}{c}
R^2 \\
R^3
\end{array}$$

$$\begin{array}{c}
(CH_2)_n \\
X
\end{array}$$

$$\begin{array}{c}
H \\
N \\
N
\end{array}$$

$$\begin{array}{c}
(I) \\
\end{array}$$

the N-oxide forms, the addition salts and the stereo-chemically isomeric forms thereof, wherein

n is 0, 1 or 2;

X is N or CR⁷, wherein R⁷ is hydrogen or taken together with R¹ may form a bivalent radical of formula -CH=CH-CH=CH-;

 R^1 is C_{1-6} alkyl or thienyl;

 R^2 is hydrogen, hydroxy, C_{1-6} alkyl, C_{3-6} alkynyl or taken together with R^3 may form =0;

R³ is a radical selected from

$$\begin{array}{lll} \text{-(CH$_2$)$_S$- NR8R^9} & \text{(a-1),} \\ \text{-O-H} & \text{(a-2),} \\ \text{-O-R$^{10}} & \text{(a-3),} \\ \text{-S- R$^{11}} & \text{(a-4), or} \\ \hline \text{-C=N} & \text{(a-5),} \end{array}$$

wherein

s is 0, 1, 2 or 3;

 $R^8 \ is \ -CHO, \ C_{1\text{--}6}alkyl, \ hydroxyC_{1\text{--}6}alkyl, \ C_{1\text{--}6}alkylcarbonyl,$

 $di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy,$

thienylC₁₋₆alkyl, pyrrolylC₁₋₆alkyl, arylC₁₋₆alkylpiperidinyl,

 $arylcarbonyl C_{1\text{--}6} alkyl,\, arylcarbonyl piperidinyl C_{1\text{--}6} alkyl,$

haloindozolylpiperidinyl $C_{1\text{--}6}$ alkyl, or

arylC₁₋₆alkyl(C₁₋₆alkyl)aminoC₁₋₆alkyl;

 R^9 is hydrogen or $C_{1\text{-}6}$ alkyl;

$$\begin{split} R^{10} \text{ is } C_{1\text{-}6} \text{alkyl}, C_{1\text{-}6} \text{alkylcarbonyl or } \text{di}(C_{1\text{-}6} \text{alkyl}) \text{amino} C_{1\text{-}6} \text{alkyl}; \text{ and } \\ R^{11} \text{ is } \text{di}(C_{1\text{-}6} \text{alkyl}) \text{amino} C_{1\text{-}6} \text{alkyl}; \end{split}$$

or R³ is a group of formula

$$-(CH_2)_f$$
-Z- (b-1),

wherein

t is 0, 1, 2 or 3;

Z is a heterocyclic ring system selected from

wherein each R^{12} independently is hydrogen, $C_{1\text{--}6}$ alkyl, aminocarbonyl, hydroxy,

—
$$C_{1-6}$$
alkanediyl— N
— C_{1-6} alkanediyl

$$\begin{split} &C_{1\text{-}6}alkyloxyC_{1\text{-}6}alkyl,\ C_{1\text{-}6}alkyloxyC_{1\text{-}6}alkylamino,\ di(phenylC_{2\text{-}6}alkenyl),\\ &piperidinylC_{1\text{-}6}alkyl,\ C_{3\text{-}10}cycloalkyl,\ C_{3\text{-}10}cycloalkylC_{1\text{-}6}alkyl,\\ &aryloxy(hydroxy)C_{1\text{-}6}alkyl,\ haloindazolyl,\ arylC_{1\text{-}6}alkyl,\ arylC_{2\text{-}6}alkenyl,\ morpholino,\\ &C_{1\text{-}6}alkylimidazolyl,\ or\ pyridinylC_{1\text{-}6}alkylamino;\ and\\ &each\ R^{13}\ independently\ is\ hydrogen,\ piperidinyl\ or\ aryl; \end{split}$$

 R^4 , R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6} alkyl, C_{1-6} alkyloxy, di(C_{1-6} alkyl)amino, di(C_{1-6} alkyl)amino C_{1-6} alkyloxy or C_{1-6} alkyloxycarbonyl; or

when R⁵ and R⁶ are on adjacent positions they may taken together form a bivalent radical of formula

-O-CH₂-O (d-1),
-O-(CH₂)₂-O- (d-2),
-CH=CH-CH=CH- (d-3), or
-NH-C(O)-NR¹⁴=CH- (d-4),
wherein R¹⁴ is
$$C_{1-6}$$
alkyl;

aryl is phenyl or phenyl substituted with halo, C₁₋₆alkyl or C₁₋₆alkyloxy;

with the proviso that when

n is 0, X is N, R^1 is C_{1-6} alkyl, R^2 is hydrogen, R^3 is a group of formula (b-1), t is 0, Z is the heterocyclic ring system (c-2) wherein said heterocyclic ring system Z is attached to the rest of the molecule with a nitrogen atom, and R^{12} is hydrogen; then at least one of the substituents R^4 , R^5 or R^6 is other than hydrogen, halo, C_{1-6} alkyl or C_{1-6} alkyloxy.

- 2. (Original) A compound as claimed in claim 1 wherein n is 0 or 1; X is N or CR⁷, wherein R⁷ is hydrogen; R¹ is C₁₋₆alkyl; R² is hydrogen; R³ is a radical selected from (a-1) or (a-2) or is group of formula (b-1); s is 0, 1 or 2; R⁸ is C₁₋₆alkyl or arylC₁₋₆alkyl(C₁₋₆alkyl)aminoC₁₋₆alkyl; t is 0, 1 or 2; Z is a heterocyclic ring system selected from (c-1), (c-2), (c-3), (c-4), (c-5) or (c-11); each R¹² independently is hydrogen or C₁₋₆alkyloxyC₁₋₆alkylamino; each R¹³ independently is hydrogen; and R⁴, R⁵ and R⁶ are each independently selected from hydrogen, halo or C₁₋₆alkyl.
- 3. (Currently Amended) A compound according to claim 1 and 2-wherein n is 0 or 1; X is N; R¹ is C₁₋₆alkyl; R² is hydrogen; R³ is a radical of formula (a-1) or is a group of formula (b-1); s is 0; R⁸ is arylC₁₋₆alkyl(C₁₋₆alkyl)aminoC₁₋₆alkyl; t is 0; Z is a heterocyclic ring system selected from (c-1) or (c-2); each R¹² independently is hydrogen or C₁₋₆alkyloxyC₁₋₆alkylamino; each R¹³ independently is hydrogen; and R⁴, R⁵ and R⁶ are each independently selected from hydrogen or halo.
- 4. (Currently Amended) A compound according to claim 1, 2 and 3 selected from compound No 5, compound No 9, compound No 2 and compound No 1:

compound 9
$$C_2H_2O_4$$
 (1:2)

compound 2
$$C_2H_2O_4$$
 (2:5); and

5. (Cancelled)

- 6. (Currently Amended) A pharmaceutical composition comprising <u>a pharmaceutically</u> acceptable carriers and as an active ingredient a therapeutically effective amount of a compound <u>according to claim 1 as claimed in claim 1 to 4</u>.
- 7. (Cancelled)
- 8. (Currently Amended) A method of treating Use of a compound for the manufacture of a medicament for the treatment in a subject of a PARP mediated disorder, comprising administering to the subject a therapeutically effective amount of wherein said compound is a compound of formula (I)

$$\begin{array}{c}
R^4 \\
R^5 \\
R^6
\end{array}$$
(CH₂)_n

$$\begin{array}{c}
H \\
N \\
N \\
\end{array}$$
(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereo-chemically isomeric forms thereof, wherein

n is 0, 1 or 2;

X is N or CR⁷, wherein R⁷ is hydrogen or taken together with R¹ may form a bivalent radical of formula -CH=CH-CH=CH-;

R¹ is C₁₋₆alkyl or thienyl;

 R^2 is hydrogen, hydroxy, C_{1-6} alkyl, C_{3-6} alkynyl or taken together with R^3 may form =O;

R³ is a radical selected from

$$-(CH_2)_S$$
- NR^8R^9 (a-1),
-O-H (a-2),
-O-R¹⁰ (a-3),
-S- R^{11} (a-4), or
— $C\equiv N$ (a-5),

wherein

s is 0, 1, 2 or 3;

R⁸ is –CHO, C₁₋₆alkyl, hydroxyC₁₋₆alkyl, C₁₋₆alkylcarbonyl,

 $di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy,$

thienylC₁₋₆alkyl, pyrrolylC₁₋₆alkyl, arylC₁₋₆alkylpiperidinyl,

arylcarbonylC₁₋₆alkyl, arylcarbonylpiperidinylC₁₋₆alkyl,

haloindozolylpiperidinylC₁₋₆alkyl, or

arylC₁₋₆alkyl(C₁₋₆alkyl)aminoC₁₋₆alkyl;

R⁹ is hydrogen or C₁₋₆alkyl;

R¹⁰ is C₁₋₆alkyl, C₁₋₆alkylcarbonyl or di(C₁₋₆alkyl)aminoC₁₋₆alkyl; and

R¹¹ is di(C₁₋₆alkyl)aminoC₁₋₆alkyl;

or R³ is a group of formula

$$-(CH_2)_t-Z-$$
 (b-1),

wherein

t is 0, 1, 2 or 3;

Z is a heterocyclic ring system selected from

HN
$$R^{12}$$
 HN R^{12} HN R^{12} HN R^{12} HN R^{12} HN R^{12} (c-4)

(c-1) (c-2) (c-3) (c-4)

$$R^{12}$$
 HN R^{12} HN R^{12} (c-5) (c-6) (c-7) R^{12} (c-8)

$$R^{13}$$
 R R^{12} (c-9) (c-10) (c-11)

wherein each R¹² independently is hydrogen, C₁₋₆alkyl, aminocarbonyl, hydroxy,

$$-C_{1\text{-}6} alkane diyl -N \\ -C_{1\text{-}6} alkane diyl \\ O$$

 C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkylamino, di(phenyl C_{2-6} alkenyl), piperidinyl C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyl C_{1-6} alkyl, aryl C_{1-6} alkyl, aryl C_{2-6} alkenyl, morpholino, C_{1-6} alkylimidazolyl, or pyridinyl C_{1-6} alkylamino; and each R^{13} independently is hydrogen, piperidinyl or aryl;

 R^4 , R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C_{1-6} alkyl, C_{1-6} alkyloxy, di(C_{1-6} alkyl)amino, di(C_{1-6} alkyl)amino C_{1-6} alkyloxy or C_{1-6} alkyloxycarbonyl; or

when R⁵ and R⁶ are on adjacent positions they may taken together form a bivalent radical of formula

-O-CH₂-O (d-1),
-O-(CH₂)₂-O- (d-2),
-CH=CH-CH=CH- (d-3), or
-NH-C(O)-NR¹⁴=CH- (d-4),
wherein R¹⁴ is
$$C_{1-6}$$
alkyl;

aryl is phenyl or phenyl substituted with halo, C₁₋₆alkyl or C₁₋₆alkyloxy.

- 9. (Cancelled)
- 10. (Currently Amended) A method for enhancing the effectiveness of chemotherapy of comprising administration of a compound according to claim 1, in a therapeutically effective amount so as to increase sensitivity of cells to chemotherapy, prior to administration of said chemotherapy Use according to claim 8 and 9 wherein the treatment involves chemosensitization.
- 11. (Currently Amended) A method for enhancing the effectiveness of radiotherapy of comprising administration of a compound according to claim 1, in a therapeutically effective amount so as to increase sensitivity of cells to ionizing radiation, prior to administration of said radiotherapy Use according to claims 8 and 9 wherein the treatment involves radiosensitization.
- 12. (Original) A combination of a compound of formula (I) with a chemotherapeutic agent

$$\begin{array}{c} R^{4} \\ R^{5} \\ R^{6} \end{array} \qquad \begin{array}{c} R^{2} \\ R^{3} \end{array} \qquad \begin{array}{c} (CH_{2})_{n} \\ X \\ \end{array} \qquad \begin{array}{c} H \\ N \\ X \\ \end{array} \qquad \begin{array}{c} (I) \\ \end{array}$$

the N-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

n is 0, 1 or 2;

X is N or CR⁷, wherein R⁷ is hydrogen or taken together with R¹ may form a bivalent radical of formula -CH=CH-CH=CH-;

 R^1 is C_{1-6} alkyl or thienyl;

 R^2 is hydrogen, hydroxy, C_{1-6} alkyl, C_{3-6} alkynyl or taken together with R^3 may form =0;

R³ is a radical selected from

$$-(CH_2)_S$$
- NR^8R^9 (a-1),
-O-H (a-2),
-O-R¹⁰ (a-3),
-S- R^{11} (a-4), or
— $C\equiv N$ (a-5),

wherein

s is 0, 1, 2 or 3;

 R^8 , R^{10} and R^{11} are each independently selected from –CHO, $C_{1\text{-}6}$ alkyl, hydroxy $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ alkylcarbonyl, amino, $C_{1\text{-}6}$ alkylamino, di($C_{1\text{-}6}$ alkyl)amino $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ alkyloxycarbonyl, $C_{1\text{-}6}$ alkylcarbonylamino $C_{1\text{-}6}$ alkyl, piperidinyl $C_{1\text{-}6}$ alkylaminocarbonyl, piperidinyl, piperidinyl $C_{1\text{-}6}$ alkyl, piperidinyl $C_{1\text{-}6}$ alkylaminocarbonyl, $C_{1\text{-}6}$ alkyloxy, thienyl $C_{1\text{-}6}$ alkyl, pyrrolyl $C_{1\text{-}6}$ alkyl, aryl $C_{1\text{-}6}$ alkylpiperidinyl, arylcarbonyl $C_{1\text{-}6}$ alkyl, arylcarbonylpiperidinyl $C_{1\text{-}6}$ alkyl, haloindozolylpiperidinyl $C_{1\text{-}6}$ alkyl, or aryl $C_{1\text{-}6}$ alkyl($C_{1\text{-}6}$ alkyl)amino $C_{1\text{-}6}$ alkyl; and

R⁹ is hydrogen or C₁₋₆alkyl;

or R³ is a group of formula

$$-(CH_2)_t$$
-Z- (b-1),

wherein

t is 0, 1, 2 or 3;

Z is a heterocyclic ring system selected from

HN
$$R^{12}$$
 HN R^{12} HN R^{12} HN R^{12} (c-1) R^{12} HN R^{12} (c-4) R^{12} HN R^{12} (c-5) R^{12} (c-6) R^{12} (c-7) R^{12} (c-8)

$$R^{13}$$
 R^{12}
 R^{12}

wherein each R¹² independently is hydrogen, halo, C₁₋₆alkyl, aminocarbonyl, amino,

 C_{1-6} alkylamino C_{1-6} alkyloxy, C_{1-6} alkyloxy C_{1-6} alkyloxy C_{1-6} alkyloxy C_{1-6} alkylamino, aryl C_{1-6} alkyl, di(phenyl C_{2-6} alkenyl), piperidinyl, piperidinyl C_{1-6} alkyl,

 C_{3-10} cycloalkyl, C_{3-10} cycloalkyl C_{1-6} alkyl, aryloxy(hydroxy) C_{1-6} alkyl, haloindazolyl, aryl C_{1-6} alkyl, aryl C_{2-6} alkenyl, aryl C_{1-6} alkylamino, morpholino, C_{1-6} alkylimidazolyl, or pyridinyl C_{1-6} alkylamino;

each R¹³ independently is hydrogen, piperidinyl or aryl;

 R^4 , R^5 and R^6 are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ alkyloxy, amino, amino $C_{1\text{-}6}$ alkyl, di($C_{1\text{-}6}$ alkyl)amino, di($C_{1\text{-}6}$ alkyl)amino $C_{1\text{-}6}$ alkyloxy or $C_{1\text{-}6}$ alkyloxycarbonyl, or $C_{1\text{-}6}$ alkyl substituted with 1, 2 or 3 substituents independently selected from hydroxy, $C_{1\text{-}6}$ alkyloxy, or amino $C_{1\text{-}6}$ alkyloxy; or

when R⁵ and R⁶ are on adjacent positions they may taken together form a bivalent radical of formula

$$-\text{O-CH}_2\text{-O}$$
 (d-1),
 $-\text{O-(CH}_2)_2\text{-O-}$ (d-2),
 $-\text{CH=CH-CH=CH-}$ (d-3), or
 $-\text{NH-C(O)-NR}^{14}\text{=CH-}$ (d-4),
wherein R^{14} is C_{1-6} alkyl;

aryl is phenyl or phenyl substituted with halo, $C_{1\text{-}6}$ alkyl or $C_{1\text{-}6}$ alkyloxy.

13. (Currently Amended) A process for preparing preparation of a compound as claimed in claim 1, comprising characterized by

a) the hydrolysis of intermediates of formula (VIII), according to art-known methods, by submitting the intermediates of formula (VIII) to appropriate reagents, such as, tinchloride, acetic acid and hydrochloric acid, in the presence of a reaction inert solvent, e.g. tetrahydrofuran.

b) the cyclization of intermediates of formula (X), according to art-known cyclizing procedures into compounds of formula (I) wherein X is CH, herein referred to as compounds of formula (I-j), and, preferably in the presence of a suitable Lewis Acid, e.g. aluminum chloride either neat or in a suitable solvent such as, for example, an aromatic hydrocarbon, e.g. benzene, chlorobenzene, methylbenzene and the like; halogenated hydrocarbons, e.g. trichloromethane, tetrachloromethane and the like; an ether, e.g. tetrahydrofuran, 1,4-dioxane and the like or mixtures of such solvents.

c) the condensation of an appropriate ortho-benzenediamine of formula (XI) with an ester of formula (XII) wherein R^h is C₁₋₆alkyl, into compounds of formula (I), wherein X is N, herein referred to as compounds of formula (I-i), in the presence of a carboxylic acid, e.g. acetic acid and the like, a mineral acid such as, for example hydrochloric acid, sulfuric acid, or a sulfonic acid such as, for example, methane-sulfonic acid, benzenesulfonic acid, 4-methylbenzenesulfonic acid and the like.